CLINICAL ARTICLE

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Analysis of Corticospinal Tract Injury by Using the Diffusion Tensor Imaging of 3.0 T Magnetic Resonance in Patients with Hypertensive Intracerebral Hemorrhage

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Objective : The purpose of this study is to identify correlations between diffusion tensor imaging(DTI) and motor improvement by quantifying and visualizing the corticospinal tract on DTI to predict motor impairment in patients with hypertensive intracerebral hemorrhage(ICH).

Methods : Fifteen normal subjects and 7 patients with hypertensive ICH were examined and the latter were treated surgically. DTI was performed with a 3.0 T MRI. The region of interest(ROI) from the posterior limbs of both internal capsules was measured on a fractional anisotropy(FA) map, and the ratios of ROIs were calculated. Tractography, 3-dimensional DTI was then constructed. Motor impairment was assessed on admission and 2weeks after stroke by the Motricity Index(MI). The FA ratio, tractography and score on MI were analyzed for correlations.

Results : The FA ratio from the initial DTI did not show a linear correlation with motor impairment. However, after 2weeks, patients with high FA ratios showed high degrees of motor recovery, regardless of the initial severity, and patients with low FA ratios showed low recovery rates. Otherwise, a relationship between the amount of hematoma and the degree of motor recovery could not be determined. On tractography, injury of the corticospinal tract could be visualized and estimated 3-dimensionally.

Conclusion : FA ratio analysis and tractography constructed from DTI may be useful in understanding corticospinal tract injury and in predicting the recovery from motor impairment in patients.

KEY WORDS : Hypertensive intracerebral hemorrhage · Diffusion tensor imaging · Corticospinal tract · Motor impairment.

Introduction

Intracerebral hemorrhage(ICH) may be accompanied by motor impairment of various degrees. The main type of motor impairment caused by ICH is injury to the motor pathway by a hematoma, particularly injury to the corticospinal tract including the internal capsule. The severity of injury differs by the size and position of the hematoma. Of several imaging methods used from an early stage of ICH to predict motor impairment, diffusion tensor imaging(DTI) has recently become the focus of much interest.

DTI is a technique used to visualize brain tissue using the directionally different diffusion occurring in different tissues, that is, the anisotropy of diffusion. This technique was introduced in 1994 by Basser et al.[2] through visualization of the anisotropic diffusion of water molecules in 3-dimensional space under a magnetic field.

The white matter of the brain, which is constructed of directionally arranged axons, shows remarkable anisotropy. Thus, the structure of white matter can be analyzed using DTI, and DTI has been used in the clinical analysis of several white matter diseases. Although the clinical application of this technique has been evaluated in patients with hypertensive or spontaneous ICH, there has been an inadequate amount of research in this area. Computed tomography (CT) and magnetic resonance imaging(MRI) can also diagnose the size and location of hematomas, but these techniques are limited in their ability to determine the relationship

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between the presence of a hematoma and damage to the corticospinal tract. Through tractography, it is possible to quantify the degree of damage to the corticospinal tract and to visualize the corticospinal tract in 3 dimensions. Therefore, it may be possible to predict motor impairment and recovery in patients with ICH using this technique.

Materials and Methods

Patient demographics

This study examined 7 patients who came into the emergency room of Keimyung University's Dongsan Medical Center between July 2003 and September 2004 with hypertensive ICH in the basal ganglia and thalamus. The subjects were 4 males and 3 females, and their average age was 49±17years. All underwent stereotactic surgery for the hematoma. The control group consisted of 15 healthy people, including 8 males and 7 females, who had no specific symptoms on neurological examination and MRI. The average age of the control group was 56±9years (Table 1).

Table 1. Clinical information in patients who underwent diffusion tensor image

Patient. No	Sex/Age	Affected side	Location	Hematoma volume(cc)	DTI time** (hours)
I	F/62	Right	BG* Thalamus	34	2
II	M/48	Right	BG	48	4
III	M/60	Right	BG	24	5
IV	F/66	Right	BG	30	12
V	M/60	Right	BG	26	27
VI	F/49	Left	BG	65	6
VII	M/32	Left	BG	38	8

*BG : basal ganglia; **DTI time : hours taken to get diffusion tensor imaging from the time of symptom onset

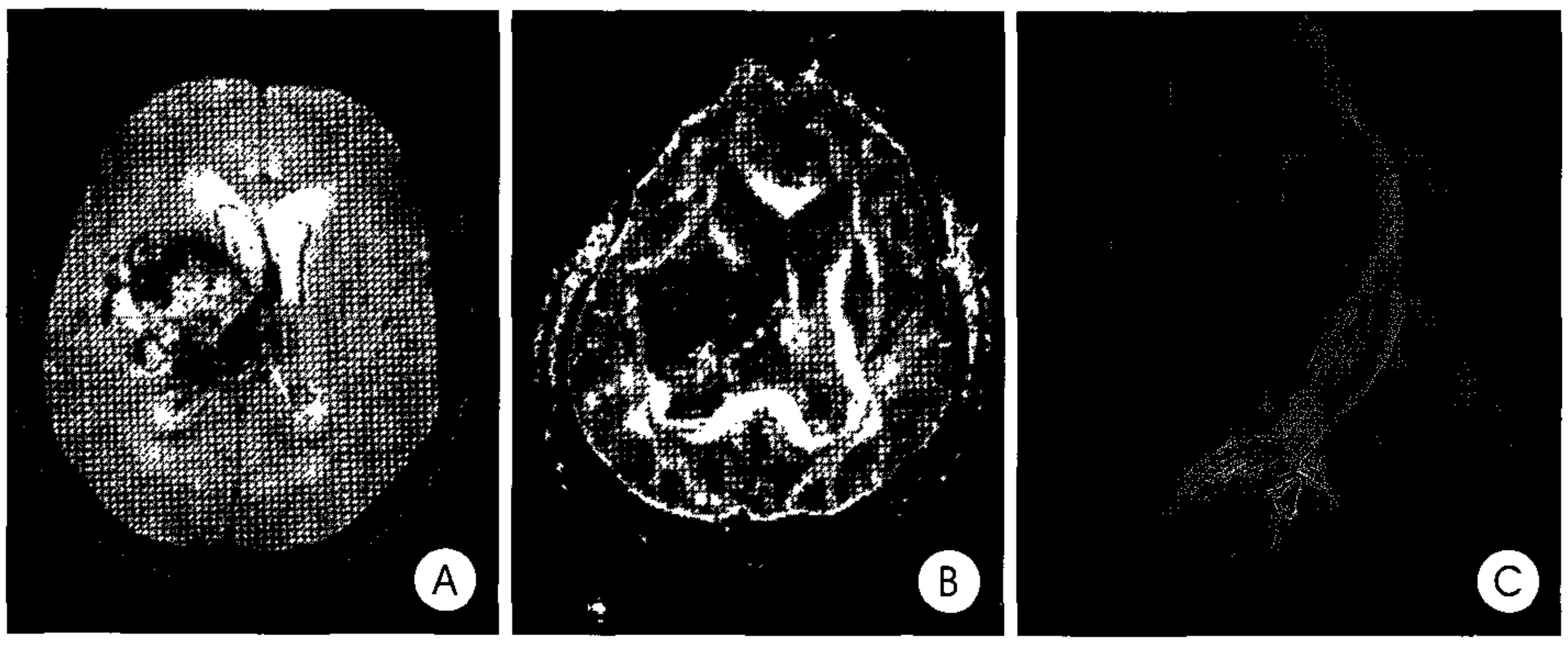

Fig. 1. Transverse images obtained from a 62-year-old woman (Patient I) show findings of hypertensive intracerebral hemorrhage at the right basal ganglia and thalamus. On a gradient echo image of magnetic resonance (A), the borders of the hematoma and internal capsule are not clear. However, on the fractional anisotropy map (B), it is possible to distinguish the posterior limb of the internal capsule from the hematoma. Note that the hematoma disrupts the posterior limb of the internal capsule. Tractography (C) shows a normal corticospinal tract including the corona radiata passing through the internal capsule on the left side, but not on the right side because it is disrupted by a hematoma on the coronal view.

Radiologic evaluation

ICH was diagnosed based on a brain CT executed in the emergency room. The amount of hematoma was calculated by recording the largest diameter seen on CT, the diameter orthogonal to it, and the number of 1-cm slices on which the hemorrhage could be seen.

The total volume was estimated using the formula for an ellipsoid, V=1/2 ABC, where A, B, and C represent the respective diameters of the 3 dimensions[28]. DTI was conducted preoperatively in all patients. On average, DTI was conducted approximately 9hours from the time of symptom onset. The DTI conditions in 3.0 T MRI (Signa VH/i General Electric Medical Systems, Milwaukee, USA) with which it was possible to execute echo planar imaging were as follows : TR 12000msec, TE minimum, FOV 240mm, NEX 1, Slice 35, Slice thickness 4mm, spacing 0mm, and Matrix 128×128. The information from these processes were analyzed after processing into a fractional anisotropy(FA) map by the Functool 2000 program (General Electric Medical Systems, Milwaukee, USA).

The FA for analyzing the extent of the injured corticospinal tract was determined by measuring the region of interest(ROI) in the FA map[22,25]. The FA was measured in the posterior limb of the internal capsule in an unaffected site (a) and in the affected site (b). The injury to the internal capsule at the affected site was determined by calculating the ratio of the affected site to the unaffected site using both FAs. In other words, the FA ratio was calculated from 'FA ratio (%)=b/a×100', and this reflected the conserved FA level of the affected site's posterior limb of the internal capsule. Using the same method, the FA was measured for the control group in the posterior limbs of both site's internal capsules using DTI. From the DTI, brain fiber tracking was performed using the free software dTV, Version 1.64 (VOL-UME-ONE, University of Tokyo Hospital, Tokyo, Japan) to compose the tractography. The seed area was set as the ROI drawn around the posterior limb of the internal capsule on the axial image of the axially reformatted FA map. Fiber tracking was stopped if the FA value was <0.18. On these images, injured nerve fibers of the affected site could be compared to those of the unaffected site by dimensional visualization. Fig. 1, 2 show gradient echo(GRE) images of MR, FA maps and tractographies of patients I and VII.

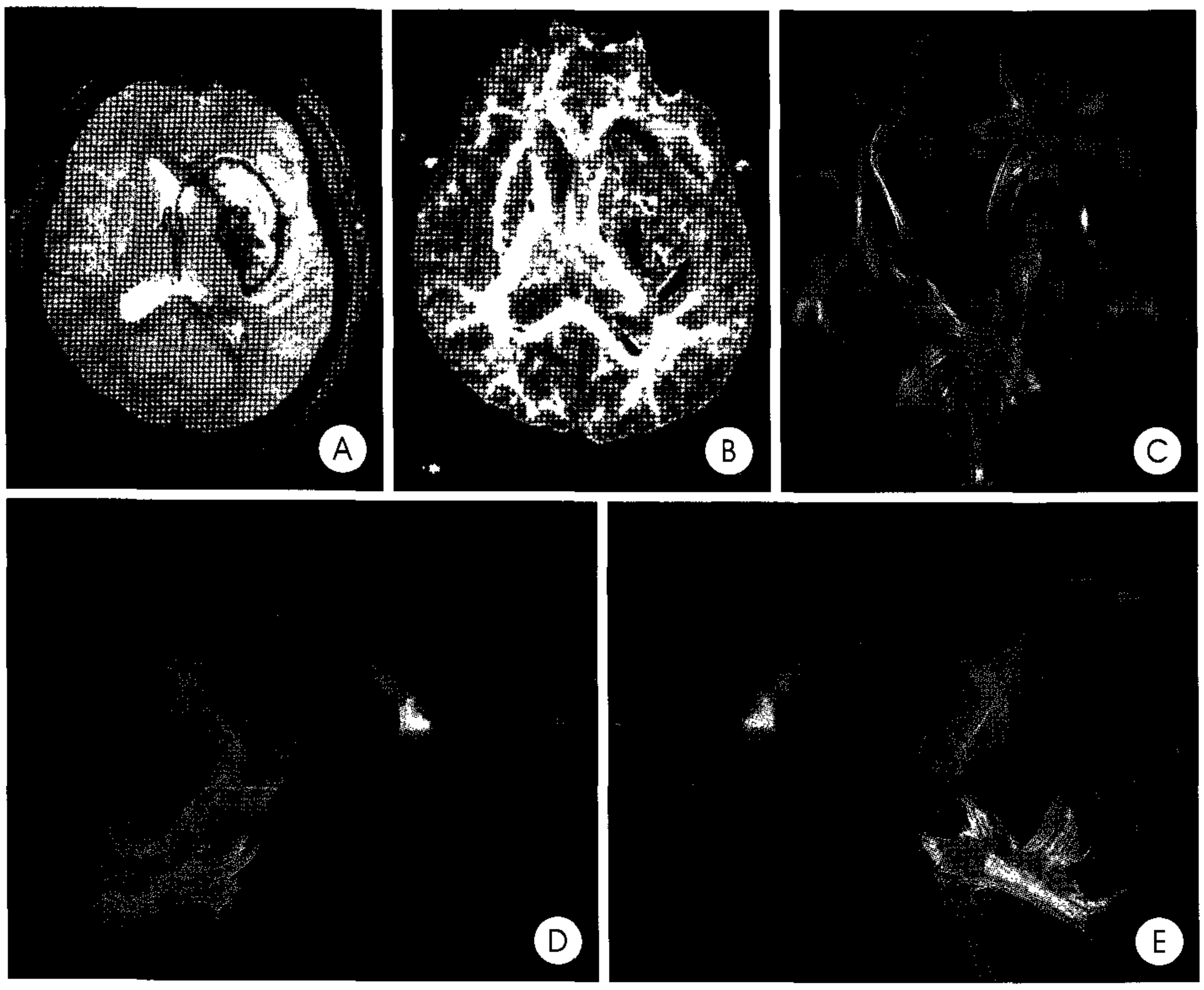

Fig. 2. Transverse images obtained from a 32-year-old man (Patient VII) show findings of hypertensive intracerebral hemorrhage at the left basal ganglia on a gradient echo image of magnetic resonance (A). On the fractional anisotropy map (B), the white matter tracts that could not be demarcated on GRE are distinguished from the hematoma. Tractography shows the corticospinal tracts from various angles, such as the coronal view (C), right sagittal view (D) and left sagittal view (E). Note that the left corticospinal tracts are a little displaced because of the hematoma.

Measurement of motor impairment

The motor function of patients was measured using the muscle strength of the upper and lower extremities as the Motricity index (MI)[6,7]. MI was examined by scoring motor function in upper and lower extremities on a 1-100 scale and comparing the score obtained in the emergency room with that obtained 2weeks later. Through DTI measuring, scores were compared and analyzed with the FA ratio and MI.

Results

The FA of the posterior limbs of the internal capsules in both the 7patients and the 15 control subjects was measured. The average FA was 0.54 in the control group and 0.56 in the patients. There was no significant difference between the controls and patients in the FA of the posterior limb of the internal capsule in the unaffected part, and the affected site's FA was decreased in all regions compared to the unaffected sites in both controls and patients. The ratios of FA in the affected part to FA in the unaffected part of the 7patients were as follows : 27.8%, 50.8%, 60.9%, 86.6%, 87.4%, 96.9% and 99.5%, and they were designated as I to VII according to the size of the FA ratio. The FA ratios of the patients and the motor power, which was measured by MI at the time of hospitalization as well as 2weeks later, are shown in Table 2.

The relationship between motor power and FA ratio of the patients at the time of hospitalization was examined. As shown in Fig. 3A, the FA ratio of patient II was the second from the lowest at 50.8%, but motor power, measured by 93 points summed from the upper and lower extremities by MI, was the second highest among all patients. On the other hand, patient VII had the highest FA ratio at 99.5%, but the lowest motor power, measured over 47points. Fig. 3B shows the relationship between motor power and FA ratios at 2weeks from the time of hospitalization. Overall motor power was slightly improved from the time of admission, but the graphical pattern was similar to that seen in Fig. 3A.

Fig. 4 shows the relationship between the extent of motor recovery after 2weeks and the FA ratio. In patients I, II and III, whose FA ratios were 27.8%, 50.8% and 60.9%, respectively, motor recovery was not found in the upper extremity, but was found in the lower extremity, with scores of 5, 9 and 9points, respectively. However, among patients with high FA ratios,

Table 2. FA ratio and motor function

Patient No.	FA			Motricity Index								
	Unaffected	Affected	FA ratio* (%)	Admission			2 Weeks			Improvement		
				U**	L***	S†	U	L	S	U	L	S
I	0.54	0.15	27.8	19	28	47	19	33	52	0	5	5
II	0.630	0.320	50.8	40	53	93	40	62	102	0	9	9
III	0.529	0.322	60.9	19	53	72	19	62	81	0	9	9
IV	0.546	0.473	86.6	29	29	58	34	43	77	5	14	19
V	0.530	0.463	87.4	61	64	125	73	76	149	12	12	24
VI	0.584	0.566	96.9	40	43	83	64	76	140	24	33	57
VII	0.564	0.561	99.5	19	28	47	50	70	120	31	42	73

*FA ratio = (FA of affected site / FA of unaffected site) x 100**U : upper extremity; ***L : lower extremity; †S : sum

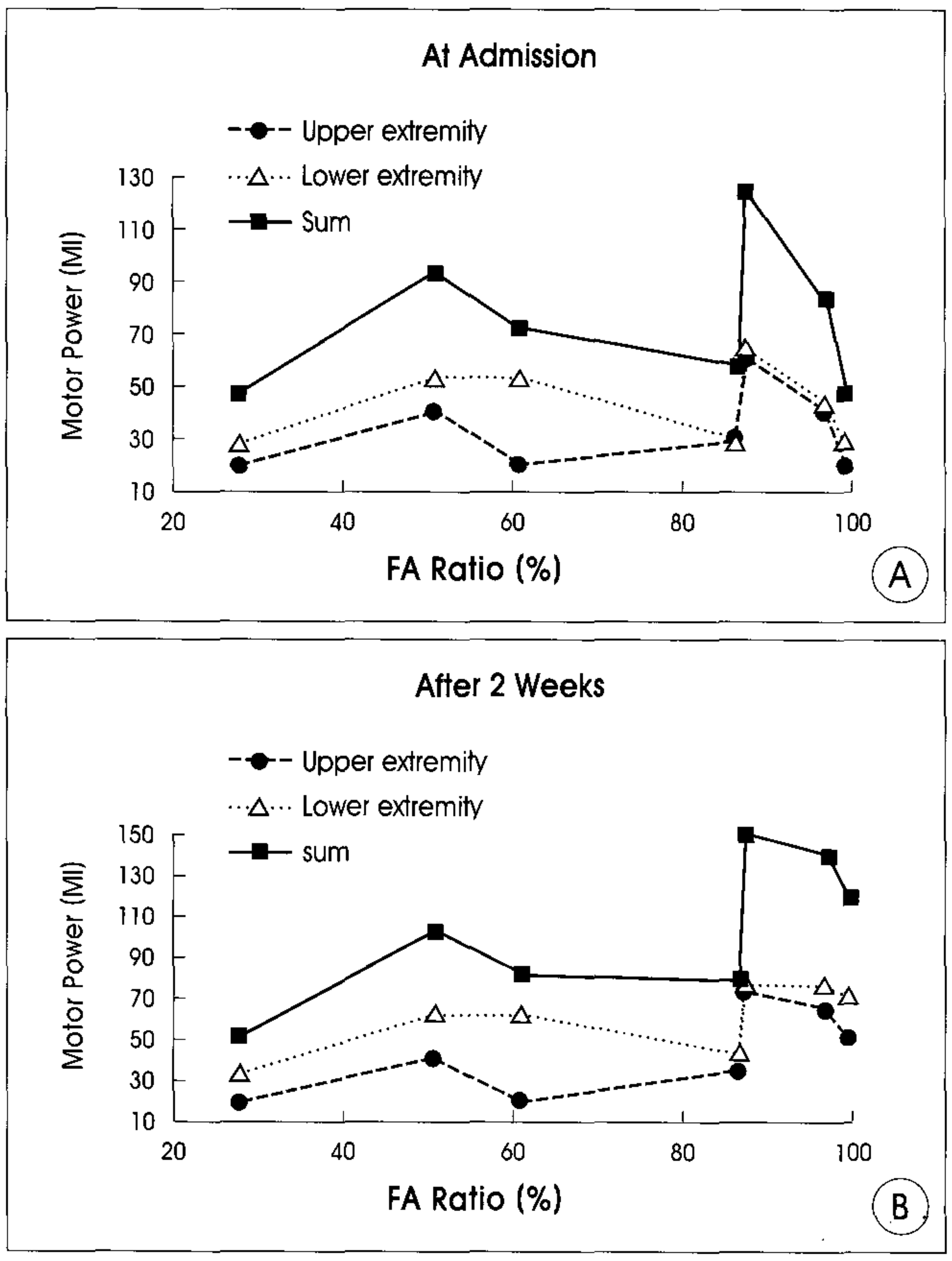

Fig. 3. The relationship between the fractional anisotropy ratio and motor power on admission and after 2weeks is graphically represented. On admission, the FA ratio did not show a proportional relationship to motor power (A). Compared to that at the time of admission, motor power was generally improved 2weeks after admission, although the graphical pattern was largely unchanged (B).

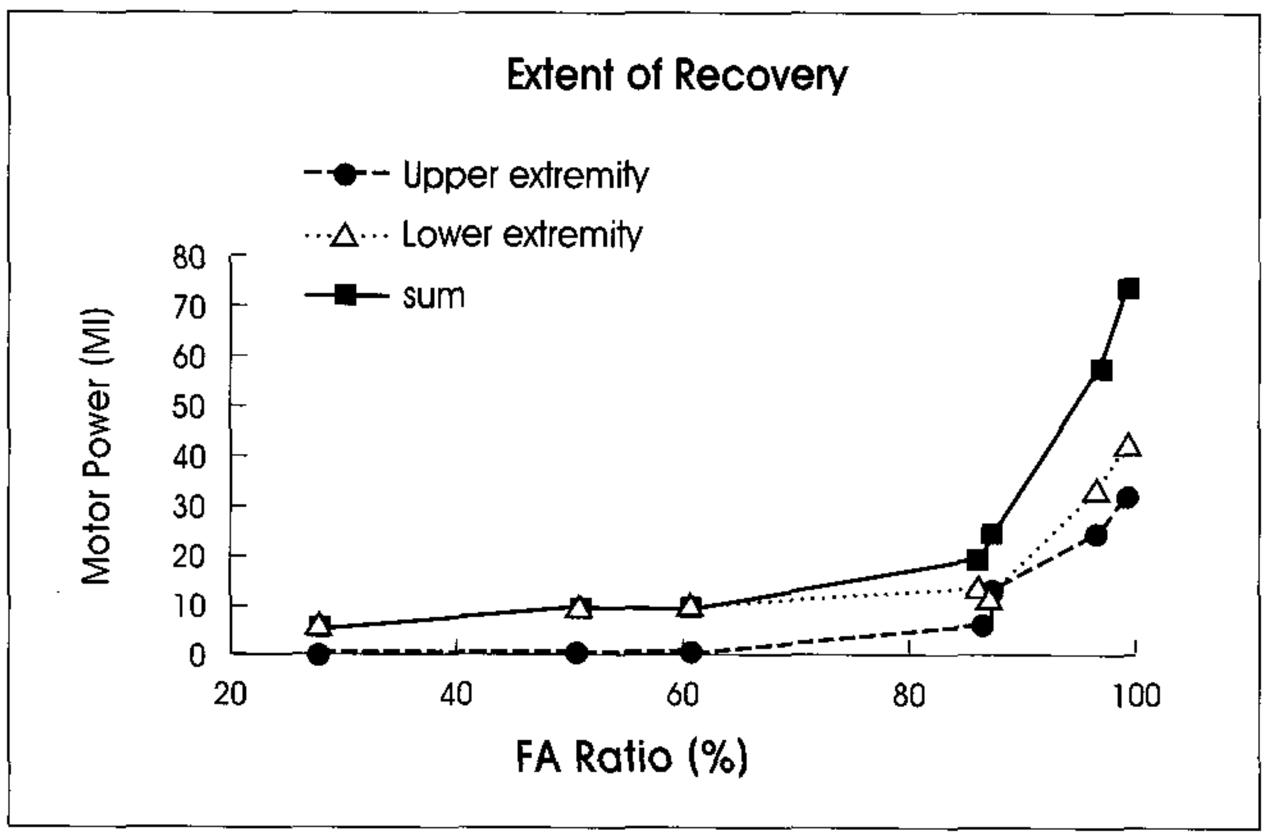

Fig. 4. The relationship of the fractional anisotropy ratio to the extent of improvement after 2weeks is graphically represented. The extent of improvement in motor power was calculated by subtracting the score on admission from the score after 2weeks. Note that the FA ratio is proportional to the extent of improvement : the higher the FA ratio, the larger the extent of improvement.

such as patients V, VI and VII, the extent of motor recovery was greater, with scores of 24, 57 and 73points, respectively.

The relationship between the amount of hematoma and motor recovery was analyzed graphically. Although patient III had the lowest amount of hematoma (24cc), the extent of motor recovery was the same as that of patient II and lower than patients IV, V, VI and VII, who each had a greater amount of hematoma. Patient VII had the largest hematoma (65cc) and showed the second largest extent of motor recovery (Fig. 5).

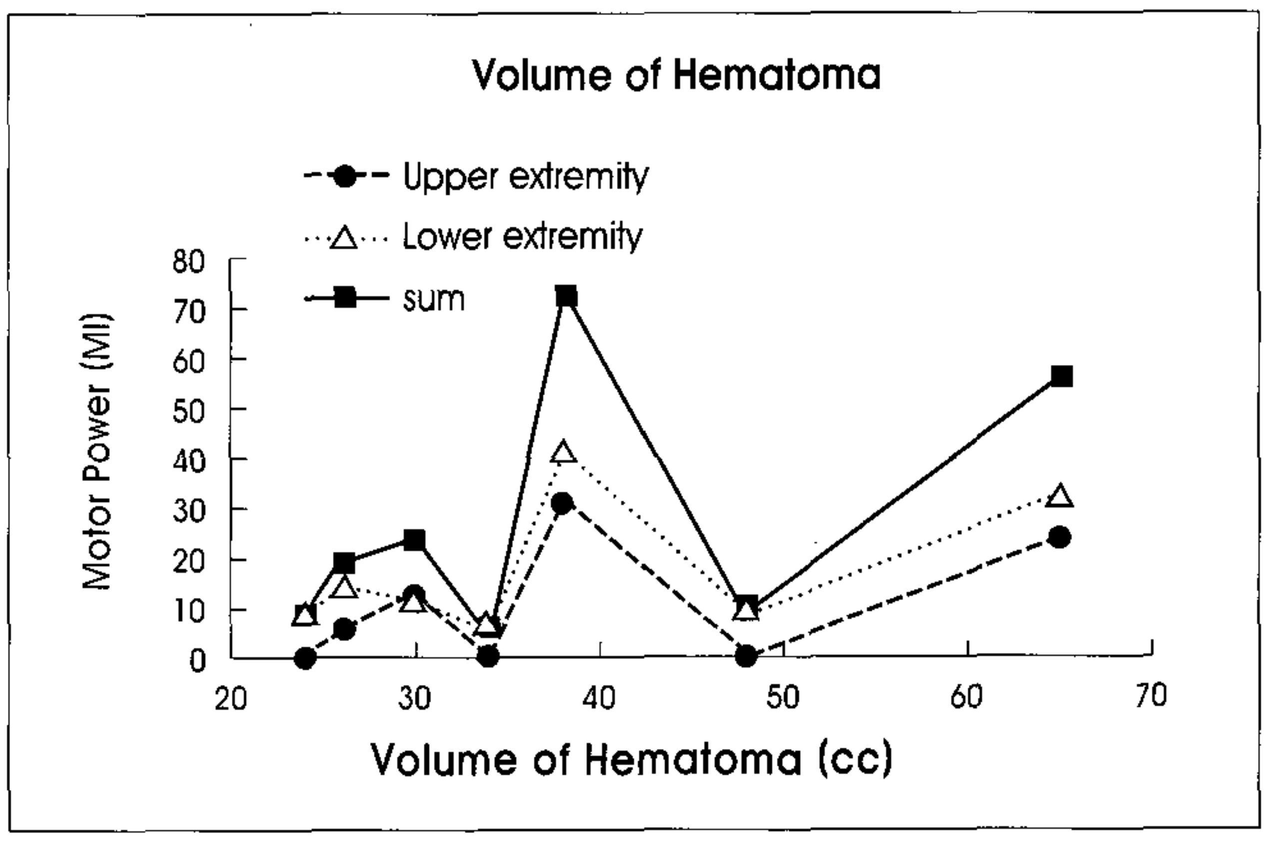

Fig. 5. The influence of the volume of hematoma on motor power is analyzed graphically. On this graph the amount of hematoma do not show a considerable influence on the extent of motor improvement.

As a result of the reconstruction of tractography, there was little corticospinal tract in the affected part relative to the unaffected part in patient I, who had a low FA ratio (Fig. 1C). On the contrary, patient VII had a high FA ratio, and almost all parts of the corticospinal tract were conserved, although there was a little displacement by hematoma (Fig. 2C, D, E).

Discussion

A water molecule in the liquid state makes an irregular micromotion called a "diffusion" that is changed by the physical environment. Diffusion-weighted MRI(DWI) is a technique which expresses the degree of diffusion occurring in biological tissues in different physical environments. DTI is a technique for visualizing different diffusion directions, called the anisotropy of diffusion. Axons are arranged in a regular direction. Therefore, white matter, which is composed of axons, shows a remarkable anisotropy[10]. Using this characteristic, it is possible to visualize white matter with strong anisotropy using DTI, allowing the structure of white matter and of a lesion invading the white matter to be easily analyzed. Therefore, DTI is widely used for visualizing and standardizing the structure of white matter[15,16]. In DTI, the relative anisotropy, FA, and volume ratio are used as standards for the anisotropic diffusion of a water molecule. Among these, the FA map is the most generally used image, with values designated from 0 for perfect isotropy to 1 for perfect anisotropy. Areas with high anisotropy, such as white matter, are shown as bright regions, while white-grey matter and CSF are dark due to their low anisotropy[13]. In measuring anisotropy of normal white matter in the FA map, the anisotropy is highest in the corpus callosum, followed by the internal capsule, optic radiation, white matter of the frontal lobe, external capsule, and white matter of the occipital lobe[24].

This method has been used in evaluating diseases of white matter based on research executed on normal white matter. In the case of cerebral infarction, DWI has been an important tool for diagnosing stroke, as its usefulness in identifying ischemia has been established[19,27]. However, DTI can provide more information than DWI due to its use of an additional magnetic field to the previous diffusion gradient given in the x, y, and z directions. Mukherjee et al.[20] found that DTI was more sensitive than DWI in the prognosis of middle cerebral artery infarction, particularly in the diagnostics of cerebral infarction of white matter. Thus, DTI has been widely used for predicting motor recovery of cerebral infarction patients. Recently, Park et al.[22] showed that there was a significant relationship between the FA ratio and the degree of upper extremity motor impairment. Moreover, white matter injury was demonstrated using DTI in patients with diffuse axonal injury who had no lesions in previous MRIs[1]. In addition, it has been asserted that connection abnormalities between the cortices is a causative factor in schizophrenia because DTI shows a small decrease of anisotropy in specific white matter in patients with schizophrenia[5]. In patients with a brain tumor, DTI has been used for planning surgical intervention and predicting symptoms through its precise visualization of the relationship between tumor and white matter[18]. It has been reported that the diffusion rate is increased and the FA ratio is decreased in white and gray matter in epilepsy patients[23]. DTI has also been used in evaluating white matter disorders, such as multiple sclerosis, Wallerian degeneration, etc.[13]

To find corticospinal tract injury by ICH and to predict motor recovery earlier, Karibe et al.[11] analyzed the anatomical distance between the corticospinal tract and hematoma in DWI. However, we used the FA ratio of DTI to more quantitatively evaluate the extent of injury of the corticospinal tract and motor recovery in patients with thalamic and putaminal hemorrhage. The FA ratio of the affected part to the unaffected part was calculated by measuring the FA of both parts in the posterior limb of the internal capsule, which is the pathway of the corticospinal tract. A high FA ratio means a more conserved corticospinal tract close to the unaffected part, and a low FA ratio indicates that the motor neuron injury is severe. In this study, we examined the relationship between the motor impairment of ICH patients and the FA ratio analyzed in DTI. Although patient VII showed the most severe initial motor impairment, he had the highest FA ratio and the highest degree of recovery. On the contrary, patient II showed the second highest initial motor power, but a lower FA ratio than other patients (except patient I), and the degree of recovery after 2weeks was lower. Although initial motor impairment was severe if the FA ratio was high, the degree of motor recovery was also high however, if the FA ratio was low and the motor impairment was not severe, there was little advancement in motor recovery. In other words, the extent of motor recovery was not related to the initial degree of motor impairment, but was related to the FA ratio.

When the relationship between the amount of hematoma and the degree of motor recovery was examined, we found a case with a small hematoma that demonstrated more severe motor impairment than was seen in the cases with large hematomas. On the other hand, there was a case with a high degree of recovery from motor impairment in spite of having a large hematoma. Therefore, the relationship between the amount of hematoma and the extent of motor recovery may not be linear. In general, if there is a large hematoma, there is the possibility of a corticospinal tract injury including the internal capsule, so the possibility of motor impairment will increase. However, when a hematoma is large, if there is no injury in the corticospinal tract, it does not directionally cause motor impairment.

Neurological recovery following stroke occurs mainly during the first 2weeks. In addition, over 90% of neurological recovery takes place by structural and functional reconstruction of neurons within 3months[21,26]. We found that in the group with FA ratios $<$50.0%, the motor power at 2weeks was about 76%, compared to that at 3months. In those with a FA ratio 50.0~75.0% or a FA ratio$>$75.0%, each group had motor power at 2weeks that reached about 82% and 100% that of 3months on the paper of Shin et al[25]. Therefore, we believe that a time frame of at least 2weeks after surgical treatment is needed to allow a decrease in the mass effect caused by bleeding and edema in order to estimate short-term recovery.

Two weeks is not a sufficient amount of time to represent long-term motor recovery. Thus, it is necessary to exclude the possibility of recoverable motor impairment by prospective structural and functional reconstruction of the corticospinal tract in this study. This should be accompanied by additional DTI and follow-up motor examinations.

There are a few additional points to be considered. There was the possibility of bias in measuring FA in this study because the boundary of measurement was not always the same in all cases. In addition, if the hematoma was included in the boundary used to measure FA, the result could show a different FA value because of the dark signal of hemosiderin. Electromyography(EMG) may be useful in increasing the objectivity and validity of the motor function evaluations.

Moreover, in examining the consistency between the damaged part of the corticospinal tract and the real motor area, functional MRI may be of help in identification. The effect of the patient's attitude regarding treatment and the existence of physical therapy should also be considered in evaluating the recovery degree and speed.

The effort to apply the DTI to the initial stage of ICH is in merely a beginning state, but the existence of a direct relationship between the FA ratio and motor impairment has been identified. DTI application has become easier and the diagnostics have been advanced in terms of accuracy, due to the high resolution imaging of thin slices and short time required to get images by generalization of 3 T-MRI[8].

Through many studies of Color-coded DTI(CDTI) of patients with stroke, it has been possible to proceed with a more detailed structural analysis of white matter, including the corticospinal tract of the motor fiber[14]. A tractography composing study has been actively examined by recomposing the DTI into 3-dimensional images using the Fiber Assignment by Continuous Tracking(FACT) method[3,12]. Mori et al.[17] determined the feasibility of tractography by comparing the anatomy of real neuronal fibers with tractography in the mouse brain. In addition, the acquisition of many pieces of valuable information obtained by composing two images from DTI and conventional MRI before surgery ofbrain tumors has been reported[4,9,29]. In this study, we composed the tractography with DTI for ICH patients.

It was observed that patients with high FA ratios had little corticospinal tract loss or just displacement, while patients with low FA ratios had severe lossof the corticospinal tract or disconnection. DTI may be developed to tractography and applied to ICH patients, as well as to white matter diseases including brain tumors. Thereby it may be possible to analyze symptoms precisely and easily through a dimensional and visual expression of the relationship between the corticospinal tract and lesions.

Conclusion

After measuring FA ratios through DTI in hypertensive ICH patients, we found that patients with high FA ratios showed high degrees of motor recovery, regardless of the initial severity of motor impairment, while patients with low FA ratios showed low recovery rates. Otherwise, a relationship between the amount of hematoma and the extent of motor recovery could not be identified. Therefore, FA ratio analysis using DTI may be helpful in predicting motor recovery in patients. In addition, tractography aided by 3-dimensional reconstruction of DTI may be useful in understanding injury of the neuronal tracts.

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Commentary

The authors investigated to identify correlations between diffusion tensor imaging(DTI) and functional motor recovery by quantifying and visualizing the corticospinal tract in 7patients with hypertensive intracerebral hemorrhage (ICH).

Recently DTI has been reported to be useful in detecting brain fiber tracking in a variety of white matter disease such as cerebral infarction, diffuse axonal injury, or neurodegenerative diseases. In results, authors summarized that the fractional anisotropy(FA) ratio which was measured 2weeks after ICH seemed to be correlated with functional motor recovery. In clinical setting, it is more important to decide whether emergency evacuation of ICH is necessary or not for the patient's motor recovery in management of ICH. However, this study showed that the initial FA ratios on admission was not helpful to predict the recovery from motor impairment in patients with ICH. It looks like some limitation of FA ratio analysis and tractography constructed from DTI in detection and localization of corticospinal tract at the acute stage of ICH.

Although further study with a large number of ICH patients will be necessary to evaluate the predictive value in motor function, FA ratio analysis used in this study might have showed some potential to predict the functional motor outcome of the patients with ICH.

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